Genetic referrals of Middle Eastern origin in a western city: inbreeding and disease profile

Elizabeth Hoodfar, Ahmad S Teebi

Abstract
Inbreeding or consanguineous marriage is a common traditional practice in Middle Eastern cultures. Studies from various countries and communities of this region showed that the frequencies range from 20% to greater than 70%. Inbreeding is known to have adverse effects on morbidity and mortality, in particular with respect to autosomal recessive disorders. This study examined 200 couples representing all referrals of Middle Eastern origin seen at a large Clinical Genetics Unit in Montreal. They were compared with a similar sized group of different cultural backgrounds from among the same referrals. The rate of intercultural marriages and inbreeding was found to be 24% and 23-5% respectively in the Middle Eastern group, while they were 22-5% and 5% in the comparison group. Excluding the referrals for consanguinity only, the rate of inbreeding among the study group was 16-4%. Within the Middle Eastern group, autosomal recessive disorders were more than twice as common in the inbred than in the non-inbred families, the pattern of which is consistent with previous observations.

(J Med Genet 1996;33:212-215)

Key words: genetic disease; inbreeding; Middle East.

The Middle East is one region of the world where inbreeding remains a commonplace practice. In western populations marriages between kin are regarded unfavourably and often limited to geographical religious isolates. In North America and western Europe the incidence of first cousin marriages is approximately 0-5%. Yet consanguineous marriages account for 20 to 50% of all unions in Middle Eastern countries. Although most of these countries are of Muslim majority, the practice of consanguinity is a cultural trait, not a religious prescription. The Quran merely permits marriages among kin no more closely related than first cousins, which also includes double first cousins. This practice stems from geographical/tribal isolation, economic benefits (of keeping land within the family), and psychosocial advantages (of knowing the spouse and his/her family well). The factors correlating with high rates of inbreeding are rural residence, lower level of education, occupational status, and social class, and young age at marriage.

With regard to health, inbreeding has an impact on the rates of reproductive loss, congenital malformations, and genetic diseases (mainly autosomal recessive conditions owing to homozygosity by descent). In general the total number of pregnancies, live births, living children, and postnatal mortality is raised among consanguineous compared to non-consanguineous couples. However, an increase in prenatal and perinatal wastage has not been consistently shown.

The rates of inbreeding have been studied among several populations in the Middle East (table 1). They range from 20-0% in Turkey to 58% in Saudi Arabia and Iraq, and up to more than 70% among the Bedouins in Kuwait. Yet for geneticists and genetic counsellors who work with large multicultural populations in North America, these figures are not readily applicable, firstly because of the heterogeneity of the country of origin, and secondly because of admixture with other populations as a result of immigration. For this reason we surveyed the rate of inbreeding among Middle Eastern couples or parents of patients who were referred to a large Genetics Unit in Montreal. This cosmopolitan city in Canada is known to have a sizeable Middle Eastern immigrant population. The goal of the study was to provide an overview of the rate and pattern of inbreeding and the spectrum of diseases observed.

Subjects and methods
The files of 3345 patients, representing all patients seen in the Genetics Unit from 1 January 1989 to 30 November 1994, were reviewed. All families with at least one parent or one

<table>
<thead>
<tr>
<th>Country/population</th>
<th>Frequency (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>40-0</td>
<td>8</td>
</tr>
<tr>
<td>Egypt</td>
<td>37-4</td>
<td>10</td>
</tr>
<tr>
<td>Iran</td>
<td>28-38</td>
<td>12</td>
</tr>
<tr>
<td>Iraq</td>
<td>24-5</td>
<td>14</td>
</tr>
<tr>
<td>Jordan</td>
<td>23-3</td>
<td>17</td>
</tr>
<tr>
<td>Kuwait</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Lebanon</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Morocco</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Palestinians in Israel</td>
<td>38-7</td>
<td>23</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Syria</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Tunisia</td>
<td>23-38</td>
<td>17</td>
</tr>
<tr>
<td>Turkey</td>
<td>23-38</td>
<td>17</td>
</tr>
</tbody>
</table>

Received 21 April 1995
Revised version accepted for publication 20 November 1995
member of the couple of Middle Eastern origin were selected as subjects for the study. Middle Eastern origin in this study was defined as countries with a Muslim majority in south-west Asia and northern Africa. All Arab countries were included as well as Iran and Turkey. In order to avoid ascertainment bias, families whose religion was cited as Christian or Jewish were not included in the study group.

A group of equal size was chosen for comparison in which neither parent or member of the couple was of Middle Eastern origin. The comparison subjects were selected by taking the file following each case subject file. Information extracted from the files of the study group and their comparisons included: country of origin of each parent or member of the couple, reason for referral, number of children, number of spontaneous abortions, number of affected sibs, other affected relatives, and presence or absence of inbreeding and its degree. When the parents/couple were found to be consanguineous, the degree of relatedness was coded.

Results
Among the files studied, 200 Middle Eastern families were found and a sample of 200 non-Middle Eastern families was obtained. The countries of origin observed among the cases were Algeria, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Morocco, Oman, Palestinian territories, Saudi Arabia, Syria, Tunisia, and Turkey. Middle Eastern subjects had a 24% rate of intercultural marriages. These marriages included those contracted across the country of origin (with non-Middle Eastern subjects or across religious boundaries with non-Muslim subjects or both). The figure for intercultural marriages was 22-5% among non-Middle Eastern families. The overall rate of inbreeding and that for various degrees of relatedness are shown in table 2. Among the Middle Eastern population of Montreal referred to the Genetics Unit, 47 unions were consanguineous. The majority of these marriages (68-1%) were between first cousins. Of the 47 couples, 17 were referred for premarital or prepregnancy counselling for consanguineous couples. By excluding this group, the rate of consanguineous marriages among the genetic referrals was 16-4%. In contrast the comparison group of non-Middle Eastern subjects had a 5-0% rate of consanguineous marriages. Of these, 70% were between first cousins.

The consanguineous couples among the comparison group originated from Armenia, Greece, Italy, Portugal, and south eastern Asian countries such as Bangladesh, India, and Sri Lanka. Only two out of 10 inbred couples were of French Canadian origin. The Middle Eastern population of Montreal has a large Lebanese component. Among the 200 cases, 84 subjects (42%) had at least one parent of Lebanese origin. Among the 47 inbred couples, 16 (34%) were of Lebanese origin.

Table 3 shows the causes of referral observed for the study group and the comparison group. While 17 out of 200 (8-5%) Middle Eastern subjects were referred specifically because of consanguinity, only one of the non-Middle Eastern subjects was referred for this reason. The overall frequency of referrals for autosomal recessive diseases was 14-5% among the study group and 19-5% among the comparison group. The number of referrals for autosomal dominant, multifactorial, and chromosomal abnormalities was comparable in the two groups.

Within the Middle Eastern group, causes of referral were compared between inbred and non-inbred subjects (table 4). Autosomal recessive conditions were more than twice as frequent among inbred cases (33-3%) than among non-inbred cases (12-4%). Autosomal recessive disorders noted among the Middle Eastern group are shown in table 5. The rate of autosomal dominant disorders was not significantly different between the two groups. However, multifactorial disorders and chromosome abnormalities appear more common among the non-inbred (25-4% and 15-7%, respectively) than inbred cases (16-6% and 6-7%).

Discussion
Our results show that, even in the west, the proportion of inbred unions continues to be raised among persons of Middle Eastern origin. Since our sample was drawn from genetic patients, the observed rate of consanguinity could in fact be slightly higher than the true rate among the general Middle Eastern population of Montreal. The fact that more than a third of the inbred families in this group were referred specifically because of consanguinity results in an increased rate of inbreeding in this...
group. The rate after excluding these families is 16.4%.

On the other hand, the rate of intercultural marriages in this Middle Eastern group is high at 24%, comparable to that seen in the non-Middle Eastern comparison group (22.5%). This observation, attributable to the effects of migration, functions to reduce the rate of inbreeding among the Middle Eastern group. Another factor with potential to lower this rate is the proportion of Lebanese subjects in the sample (42%). As table 1 shows, the Lebanese population has one of the lower frequencies of inbreeding in the Middle East.

Looking at the disease profile, there is an apparent increase of autosomal recessive disorders among inbred compared to non-inbred Middle Eastern subjects. This is consistent with theoretical prediction and observation.33 The pattern of autosomal recessive disorders in the Middle Eastern group is consistent with the pattern seen among mixed Arab populations.31 Some relatively common disorders observed among this population are also seen in the study group. These include the adrenogenital syndrome, argininosuccinic aciduria, familial Mediterranean fever, Gaucher disease type 1, gangliosidosis, haemoglobinopathies, sensorineural deafness, tyrosinaemia, and Werdnig-Hoffmann disease. Surprisingly, the overall proportion of referrals for autosomal recessive disorders is slightly less in the Middle Eastern groups than in the comparison group. For multifactorial conditions there is no overall difference between the two samples. Within the Middle Eastern group, multifactorial conditions and chromosomal abnormalities are less common among the inbred than the non-inbred families. However, because the sample size of inbred families (n = 30) is small, the results are not conclusive.

### Table 4 Referrals for Middle Eastern families

<table>
<thead>
<tr>
<th>Cause of referral</th>
<th>Consanguineous</th>
<th>Non-consanguineous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive disorders</td>
<td>10 (33.3%)</td>
<td>19 (62.4%)</td>
</tr>
<tr>
<td>Autosomal dominant disorders</td>
<td>6 (20%)</td>
<td>30 (9.6%)</td>
</tr>
<tr>
<td>X linked disorders</td>
<td>2 (6.7%)</td>
<td>5 (3.3%)</td>
</tr>
<tr>
<td>Multifactorial disorders</td>
<td>5 (16.6%)</td>
<td>30 (25.4%)</td>
</tr>
<tr>
<td>Chromosome abnormalities</td>
<td>2 (6.7%)</td>
<td>24 (15.7%)</td>
</tr>
<tr>
<td>Teratology</td>
<td>0</td>
<td>20 (2.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (13.3%)</td>
<td>33 (21.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>153</td>
</tr>
</tbody>
</table>

* Excludes those referred for consanguinity.

### Conclusion

In western multicultural cities, an understanding of the factors influencing the genetic disease profile of the population is important. This knowledge is crucial for geneticists and genetic counsellors in their evaluation, diagnosis, counselling, and management of patients. One of the most important factors influencing the genetic profile of this group is the high rate of inbreeding. Our survey showed that in a genetic unit this rate is between 16-4%, and that among inbred families autosomal recessive diseases are more than twice as likely. These results are useful, not only for Montreal's genetic health professionals and researchers, but also for those dealing with Arab and Middle Eastern patients elsewhere in North America and Europe.

We thank Dr Muin Khoury from the Division of Birth Defects, CDC Atlanta for reading the manuscript and for his useful suggestions. We also thank Barbara Mazzer of the McGill Department of Epidemiology for her help in study design and research methodology and Susan Laurie for her help in retrieving patients' files and preparing the manuscript.

Genetic referrals of Middle Eastern origin in a western city

Genetic referrals of Middle Eastern origin in a western city: inbreeding and disease profile.

E Hoodfar and A S Teebi

doi: 10.1136/jmg.33.3.212

Updated information and services can be found at:
http://jmg.bmj.com/content/33/3/212

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/